

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference KR/DM/P32181	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/EP 99/ 08704	International filing date (day/month/year) 08/11/1999	(Earliest) Priority Date (day/month/year) 12/11/1998
Applicant SMITHKLINE BEECHAM P.L.C. et al.		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 5 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the language, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international search was carried out on the basis of the sequence listing:

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

2. ☒ Certain claims were found unsearchable (See Box I).

3. ☐ Unity of invention is lacking (see Box II).

4. With regard to the title,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

PHARMACEUTICAL COMPOSITION FOR MODIFIED RELEASE OF AN INSULIN SENSITISER AND ANOTHER ANTIDIABETIC AGENT

5. With regard to the abstract,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the drawings to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

national application No.

PCT/EP 99/ 08704

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP 99/08704

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/353 A61K31/4439 A61K9/32 A61K9/52 A61K45/06
A61P3/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 861 666 A (TAKEDA CHEMICAL INDUSTRIES LTD) 2 September 1998 (1998-09-02) page 10, line 3 - line 31 page 11 -page 12; examples 1,2 page 8, line 39 - line 57 page 9, line 39 - line 55 claims 12,13,15,24,26	1-6, 8-11, 15-18
X	WO 98 11884 A (KNOLL AG ;BAILEY CLIFFORD JAMES (GB); JACKSON HELEN CHRISTINE (GB)) 26 March 1998 (1998-03-26) page 4, line 20 -page 5, line 3 page 12, line 29 -page 13, line 7 claims 21-25	1-6, 8-11,15, 17,18
	-/-	

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"Z" document member of the same patent family

Date of the actual completion of the international search

3 April 2000

Date of mailing of the international search report

07/04/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Muller, S

INTERNATIONAL SEARCH REPORT

International Application No.

PCT/EP 99/08704

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 42340 A (CIRD GALDERMA ;FANJOL ANDREA (US); PFAHL MAGNUS (US); LERNHARDT WA) 1 October 1998 (1998-10-01) abstract claims 1-15	1-6, 10, 15
X	US 5 502 078 A (HOLLOWAY BRIAN R ET AL) 26 March 1996 (1996-03-26)	1-6, 10, 11
Y	column 3, line 32 - line 53	13, 14
Y	DE 44 32 757 A (BOEHRINGER MANNHEIM GMBH) 21 March 1996 (1996-03-21) page 3, line 41 -page 4, line 31 page 7 -page 8; example 4	13, 14
P, X	WO 99 03477 A (BUCKINGHAM ROBIN EDWIN ;SMITH STEPHEN ALISTAIR (GB); SMITHKLINE BE) 28 January 1999 (1999-01-28) page 2, line 19 -page 3, line 2 page 6, line 13 -page 7, line 18 page 10 claims 1-22	1-6, 15, 17-19

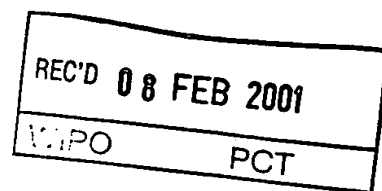
INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 99/08704

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP 0861666 A	02-09-1998	AU 5603496 A	09-01-1997
		CA 2179584 A	21-12-1996
		CN 1145783 A	26-03-1997
		CZ 9601811 A	15-01-1997
		EP 0749751 A	27-12-1996
		HU 9601698 A	28-05-1997
		JP 9067271 A	11-03-1997
		JP 10167986 A	23-06-1998
		NO 962606 A	23-12-1996
		SK 79496 A	08-01-1997
		US 5965584 A	12-10-1999
		US 5952356 A	14-09-1999
WO 9811884 A	26-03-1998	AU 4774097 A	14-04-1998
		CN 1237905 A	08-12-1999
		CZ 9900936 A	11-08-1999
		EP 0927028 A	07-07-1999
		HR 970505 A	31-08-1998
		NO 991358 A	19-03-1999
		PL 332305 A	30-08-1999
WO 9842340 A	01-10-1998	AU 6576398 A	20-10-1998
		NO 994612 A	24-11-1999
US 5502078 A	26-03-1996	AT 128116 T	15-10-1995
		AU 653229 B	22-09-1994
		AU 1704392 A	03-12-1992
		CA 2068378 A	29-11-1992
		CN 1069022 A	17-02-1993
		CS 9201591 A	16-12-1992
		DE 69204908 D	26-10-1995
		DE 69204908 T	08-02-1996
		DK 516350 T	04-12-1995
		EP 0516350 A	02-12-1992
		ES 2077354 T	16-11-1995
		FI 922423 A	29-11-1992
		GR 3017681 T	31-01-1996
		HU 61968 A	29-03-1993
		HU 211732 B	28-12-1995
		JP 6087801 A	29-03-1994
		MW 2392 A	10-03-1993
		MX 9202501 A	01-11-1992
		NO 922114 A	30-11-1992
		NZ 242642 A	22-12-1994
		PL 294705 A	26-07-1993
		RO 111457 A	31-10-1996
		ZA 9203355 A	28-04-1993
		ZW 7292 A	03-02-1993
DE 4432757 A	21-03-1996	AU 3567295 A	29-03-1996
		WO 9608243 A	21-03-1996
		EP 0781129 A	02-07-1997
		JP 10505604 T	02-06-1998
		US 5955106 A	21-09-1999
WO 9903477 A	28-01-1999	AU 8448898 A	10-02-1999



INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)



Applicant's or agent's file reference KR/P32181	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/EP99/08704	International filing date (day/month/year) 08/11/1999	Priority date (day/month/year) 12/11/1998
International Patent Classification (IPC) or national classification and IPC A61K31/353		
Applicant SMITHKLINE BEECHAM P.L.C. et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 7 sheets, including this cover sheet.
☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☒ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 30/05/2000	Date of completion of this report 05.02.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer Greif, G Telephone No. +49 89 2399 8659 

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP99/08704

I. Basis of the report

1. This report has been drawn on the basis of *(substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to the report since they do not contain amendments (Rules 70.16 and 70.17).)*

Description, pages:

1-18 as originally filed

Claims, No.:

1-19 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP99/08704

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
- ☒ claims Nos. 1-11, 13-14 (all in parts), 12.

because:

- ☒ the said international application, or the said claims Nos. 12; see separate sheet Item III, paragraph 1 relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the said claims Nos. 1-11, 13-14 (in parts).
2. A meaningful international preliminary examination report cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:
- ☐ the written form has not been furnished or does not comply with the standard.
- ☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	7, 13-14 (all in parts); 19
	No:	Claims	1-6, 8-11, 15-18
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-11, 13-19
Industrial applicability (IA)	Yes:	Claims	1-11, 13-19

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/EP99/08704

No: Claims

2. Citations and explanations
see separate sheet

VI. Certain documents cited

1. Certain published documents (Rule 70.10)

and / or

2. Non-written disclosures (Rule 70.9)

see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

R Item III**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. No opinion can be established of claim 12, since claim 12 is missing in the application.
2. Claims 1-11 and 13-14 relate to compounds defined by reference to a desirable characteristic or property, namely an insulin sensitizer and an antidiabetic agent. Since the application provides support within the meaning of Art. 6 PCT and/or disclosure within the meaning of Art. 5 PCT only for a limited number of such compounds, the search has been carried out for the parts of the claims that relate to the compounds in claims 15-19, and to the concepts of "insulin sensitizer" and "antidiabetic agent".

Under Rule 66.1(e)EPC, a preliminary examination is not carried out on matter which has not been searched. Therefore, the preliminary examination has been carried out on the whole subject-matter of claims 15-19, and on the parts of claims 1-11 and 13-14 that have been searched.

Re Item V**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. The opinion expressed as to novelty, inventive step and industrial applicability refers only to matter for which an international search report has been drawn up (Rule 66.1(e) PCT).

The assessment of the claims of the present application with regard to novelty, inventive step and industrial applicability is done under the assumption that the priority of the present application is validly claimed.

2. Reference is made to the following documents:

D1: EP-A-0 861 666

D2: DE 44 32 757 A

3. Novelty

D1 discloses pharmaceutical compositions comprising an insulin sensitizer such as pioglitazone or troglitazone, together with another antidiabetic such as an a-

glucosidase inhibitor such as voglibose, a biguanide such as metformin or phenformin, an insulin secretagogue such as glibenclamide, the oral dosage forms being coated for enteric dissolution or sustained release, the coating material including hydroxymethylcellulose phthalate or Eudragit (p. 8, lines 32-57; p. 9, lines 39-55; p. 10, lines 3-31; Examples 1 and 2; claims 12, 13, 15, 24 and 26). **D1** is therefore novelty destroying for claims 1-6, 8-11, and 15-18 of the present application.

Claims 7, 13-14 and 19 contain novel subject-matter.

4. Inventive Step

Dependent claims 7 and 13-14 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of inventive step, because the pharmaceutical formulations that represent the subject-matter of said claims come within the scope of the customary practice followed by persons skilled in the art, especially as the advantages thus achieved can readily be foreseen. Furthermore, **D2** discloses multilayer tablets with enteric coating, and by using methylcellulose, hydroxypropyl methylcellulose phthalate, Eudragit to achieve sustained release (p. 3, lines 41-67), and would therefore provide the person skilled in the art with suitable substances to prepare sustained release matrixes of disintegrating or non-disintegrating type.

The subject-matter of claim 19 is not inventive for the following reason: The activity of the secretagogue repaglinide is considered state of the art as are the compounds cited in claim 18. The expert in the field would not hesitate to use the secretagogues from either claim 18 or 19, especially since there is no indication in the present application that the use of repaglinide or nateglinide in combination with compound I of the present application has an unexpected effect over the compositions described in claim 18.

5. Industrial Applicability

Claims 1-11 and 13-19 of the present application fulfill the requirements of the PCT with respect to industrial applicability.

EXAMINATION REPORT - SEPARATE SHEET

Re Item VI**Certain documents cited**

Certain published documents (Rule 70.10)

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 99/03477	28.1.1999	16.7.1998	18.7.1997

Re Item VII**Certain defects in the international application**

Claim 12 is missing. Rule 6.1(b) PCT states that claims should be numbered in a consecutive manner with Arabic numerals.

Re Item VIII**Certain observations on the international application**

1. The identity of "Compound (I)", which appears to define an insulin sensitizer, used in Claim 2 and dependent claims, has not been disclosed in said claims or any other claim. Independent claim 2 therefore contains a reference to the description. According to Rule 6.2(a) PCT, claims should not contain such references except where absolutely necessary, which is not the case here.
2. Although claims 16-19 are dependent claims, the terms "alpha glucosidase inhibitor" (claim 16), "biguanide" (claim 17) and "insulin secretagogue" (claims 18 and 19) have not been mentioned in any of the previous claims 1-15 that claim 16-19 depend on.



INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : A61K 31/353, 31/4439, 9/32, 9/52, 45/06, A61P 3/10		A1	(11) International Publication Number: WO 00/28989
			(43) International Publication Date: 25 May 2000 (25.05.00)
(21) International Application Number: PCT/EP99/08704		RE, Vincenzo [GB/GB]; SmithKline Beecham Pharmaceuticals, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB).	
(22) International Filing Date: 8 November 1999 (08.11.99)		(74) Agent: RUTTER, Keith; SmithKline Beecham Corporate Intellectual Property, Two New Horizons Court, Brentford, Middlesex TW8 9EP (GB).	
(30) Priority Data:		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).	
9824866.9 12 November 1998 (12.11.98) GB 9824867.7 12 November 1998 (12.11.98) GB 9824869.3 12 November 1998 (12.11.98) GB 9912193.1 25 May 1999 (25.05.99) GB 9912190.7 25 May 1999 (25.05.99) GB 9912191.5 25 May 1999 (25.05.99) GB			
(71) Applicant (for all designated States except US): SMITHKLINE BEECHAM P.L.C. [GB/GB]; New Horizons Court, Brentford, Middlesex TW8 9EP (GB).			
(72) Inventors; and			
(75) Inventors/Applicants (for US only): LEWIS, Karen [GB/GB]; SmithKline Beecham Pharmaceuticals, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). LILLIOTT, Nicola, Jayne [GB/GB]; SmithKline Beecham Pharmaceuticals, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB). MACKENZIE, Donald, Colin [GB/GB]; SmithKline Beecham Pharmaceuticals, New Frontiers Science Park South, Third Avenue, Harlow, Essex CM19 5AW (GB).		Published <i>With international search report.</i> <i>Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.</i>	
(54) Title: PHARMACEUTICAL COMPOSITION FOR MODIFIED RELEASE OF AN INSULIN SENSITISER AND ANOTHER ANTIDIABETIC AGENT			
(57) Abstract			
<p>A pharmaceutical composition, which composition comprises: an insulin sensitiser and another antidiabetic agent and a pharmaceutically acceptable carrier therefor, wherein the composition is arranged to provide a modified release of at least one of the insulin sensitiser and the other antidiabetic agent, and the use of such composition in medicine.</p>			

FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

INTERNATIONAL SEARCH REPORT

I. National Application No

PCT/EP 99/08704

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/353 A61K31/4439 A61K9/32 A61K9/52 A61K45/06
A61P3/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 861 666 A (TAKEDA CHEMICAL INDUSTRIES LTD) 2 September 1998 (1998-09-02) page 10, line 3 - line 31 page 11 -page 12; examples 1,2 page 8, line 39 - line 57 page 9, line 39 - line 55 claims 12,13,15,24,26 ---	1-6, 8-11, 15-18
X	WO 98 11884 A (KNOLL AG ;BAILEY CLIFFORD JAMES (GB); JACKSON HELEN CHRISTINE (GB)) 26 March 1998 (1998-03-26) page 4, line 20 -page 5, line 3 page 12, line 29 -page 13, line 7 claims 21-25 --- -/-	1-6, 8-11,15, 17,18

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

3 April 2000

Date of mailing of the international search report

07/04/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Muller, S

INTERNATIONAL SEARCH REPORT

I. International Application No

PCT/EP 99/08704

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 42340 A (CIRD GALDERMA ;FANJOL ANDREA (US); PFAHL MAGNUS (US); LERNHARDT WA) 1 October 1998 (1998-10-01) abstract claims 1-15 ---	1-6,10, 15
X	US 5 502 078 A (HOLLOWAY BRIAN R ET AL) 26 March 1996 (1996-03-26) column 3, line 32 - line 53 ---	1-6,10, 11
Y		13,14
Y	DE 44 32 757 A (BOEHRINGER MANNHEIM GMBH) 21 March 1996 (1996-03-21) page 3, line 41 -page 4, line 31 page 7 -page 8; example 4 ---	13,14
P,X	WO 99 03477 A (BUCKINGHAM ROBIN EDWIN ;SMITH STEPHEN ALISTAIR (GB); SMITHKLINE BE) 28 January 1999 (1999-01-28) page 2, line 19 -page 3, line 2 page 6, line 13 -page 7, line 18 page 10 claims 1-22 -----	1-6,15, 17-19

INTERNATIONAL SEARCH REPORT

International application No.

PCT/EP 99/08704

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 99/08704

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0861666	A	02-09-1998	AU 5603496 A	09-01-1997
			CA 2179584 A	21-12-1996
			CN 1145783 A	26-03-1997
			CZ 9601811 A	15-01-1997
			EP 0749751 A	27-12-1996
			HU 9601698 A	28-05-1997
			JP 9067271 A	11-03-1997
			JP 10167986 A	23-06-1998
			NO 962606 A	23-12-1996
			SK 79496 A	08-01-1997
			US 5965584 A	12-10-1999
			US 5952356 A	14-09-1999
WO 9811884	A	26-03-1998	AU 4774097 A	14-04-1998
			CN 1237905 A	08-12-1999
			CZ 9900936 A	11-08-1999
			EP 0927028 A	07-07-1999
			HR 970505 A	31-08-1998
			NO 991358 A	19-03-1999
			PL 332305 A	30-08-1999
WO 9842340	A	01-10-1998	AU 6576398 A	20-10-1998
			NO 994612 A	24-11-1999
US 5502078	A	26-03-1996	AT 128116 T	15-10-1995
			AU 653229 B	22-09-1994
			AU 1704392 A	03-12-1992
			CA 2068378 A	29-11-1992
			CN 1069022 A	17-02-1993
			CS 9201591 A	16-12-1992
			DE 69204908 D	26-10-1995
			DE 69204908 T	08-02-1996
			DK 516350 T	04-12-1995
			EP 0516350 A	02-12-1992
			ES 2077354 T	16-11-1995
			FI 922423 A	29-11-1992
			GR 3017681 T	31-01-1996
			HU 61968 A	29-03-1993
			HU 211732 B	28-12-1995
			JP 6087801 A	29-03-1994
			MW 2392 A	10-03-1993
			MX 9202501 A	01-11-1992
			NO 922114 A	30-11-1992
			NZ 242642 A	22-12-1994
			PL 294705 A	26-07-1993
			RO 111457 A	31-10-1996
			ZA 9203355 A	28-04-1993
			ZW 7292 A	03-02-1993
DE 4432757	A	21-03-1996	AU 3567295 A	29-03-1996
			WO 9608243 A	21-03-1996
			EP 0781129 A	02-07-1997
			JP 10505604 T	02-06-1998
			US 5955106 A	21-09-1999
WO 9903477	A	28-01-1999	AU 8448898 A	10-02-1999

INTERNET COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Assistant Commissioner for Patents
United States Patent and Trademark
Office
Box PCT
Washington, D.C.20231
ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 28 June 2000 (28.06.00)	
International application No. PCT/EP99/08704	Applicant's or agent's file reference KR/DM/P32181
International filing date (day/month/year) 08 November 1999 (08.11.99)	Priority date (day/month/year) 12 November 1998 (12.11.98)
Applicant LEWIS, Karen et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
30 May 2000 (30.05.00)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

<p>The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No.: (41-22) 740.14.35</p>	<p>Authorized officer C. Villet</p> <p>Telephone No.: (41-22) 338.83.38</p>
--	---